Management of Asthma and COPD Exacerbations in Adults in the ICU

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Severe, life-threatening asthma and COPD exacerbations are managed commonly in the ICU and are associated with significant morbidity and mortality. It is important to understand the commonalities and differences in the diagnosis and management of these obstructive lung diseases to improve patient outcomes via evidence-based care. In this review, we first outline triggers of acute asthma and COPD exacerbations and an initial diagnostic evaluation and severity assessment. We then review the pathophysiologic features of asthma and COPD exacerbations and create a framework for the management of exacerbations in critically ill adult patients aimed at reducing airway inflammation, reversing bronchospasm, and, in severe cases, supporting patients with mechanical ventilation or advanced therapies until clinical improvement is achieved.

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KEY WORDS: asthma; asthma exacerbation; bronchodilator; COPD; COPD exacerbation; corticosteroids; critical care; ECMO; mechanical ventilation; noninvasive ventilation

CLINICAL QUESTION

A 35-year-old man with a history of poorly controlled asthma seeks treatment at the emergency department because of shortness of breath and chest tightness, diagnosed as an asthma exacerbation. Despite treatment with nebulized bronchodilators and IV corticosteroids, he remains in severe respiratory distress with acute hypercapnia, prompting urgent intubation. His initial ventilator settings in a volume control mode are: tidal volume, 400 mL; respiratory rate, 30 breaths/min; F_{IO_2}, 40%; and positive end expiratory pressure (PEEP), 5 cm H_2O. Shortly after arrival to the ICU, he becomes acutely hypoxemic, hypotensive, and tachycardic. Bedside ultrasound reveals lung sliding bilaterally and normal cardiac function without evidence of tamponade. The endotracheal tube is disconnected from the ventilator and the patient is allowed to exhale fully. The hemodynamic features improve and the endotracheal tube is reconnected to the ventilator.

Which of the following should be adjusted to prevent this from occurring again?

A. Increase the inspiratory to expiratory ratio

B. Decrease the respiratory rate

C. Increase the F_{IO_2}

D. Prone positioning

(See Answer/Rationale at the end of the article)

ABBREVIATIONS: ECMO = extracorporeal membrane oxygenation; ED = emergency department; heliox = helium-oxygen; HFNT = high-flow nasal therapy; IMV = invasive mechanical ventilation; LOS = length of stay; NIV = noninvasive ventilation; $Paco_2$ = arterial carbon dioxide tension; PEEP = positive end-expiratory pressure; PEEPi = intrinsic positive end-expiratory pressure; P_{plat} = plateau airway pressure; RCT = randomized controlled trial; RR = respiratory rate; SABA = short-acting β-agonist; SAMA = short-acting muscarinic antagonist; V_T = tidal volume; $\dot{V}/\dot{Q}$ = ventilation/perfusion

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Key Points

1. Prednisone 40 to 50 mg/d (or equivalent) is indicated for 5 to 7 days in asthma exacerbations and for 5 days in COPD exacerbations. Higher doses can be considered on a case-by-case basis; however, very high doses (ie, methylprednisolone > 240 mg/d) should be avoided because of an increased risk of treatment failure, hyperglycemia, and fungal infections.
2. Noninvasive ventilation (NIV) is recommended as the initial method of mechanical ventilation in COPD exacerbations and should be considered cautiously in severe asthma exacerbations.
3. Among patients requiring invasive mechanical ventilation, plateau airway pressure (P_{plat}) and intrinsic positive end-expiratory pressure should be monitored as indicators of hyperinflation with the goal of maintaining P_{plat} of < 30 cm H_2O.
4. Use of NIV or high-flow nasal therapy immediately after extubation reduces the risk of reintubation in COPD exacerbations, but these therapies do not have a clear role in asthma exacerbations.
5. After initiation of venovenous extracorporeal membrane oxygenation for a life-threatening asthma or COPD exacerbation with hypercapnic respiratory failure, arterial carbon dioxide tension ($Paco_2$) should not be reduced by > 20 mm Hg or 50% of the $Paco_2$ before treatment (whichever is less) within the first day to avoid neurologic complications.

Introduction

Asthma and COPD are the most common chronic respiratory diseases in the world, affecting approximately 20 million and 14 million US adults, respectively.[1-3] Each year, hundreds of thousands of asthma and COPD exacerbations require hospitalization, of which an estimated 10% to 19% are managed in the ICU.[4,5] Severe exacerbations requiring the ICU are associated with significant morbidity and mortality, with rates as high as 25% to 30% among patients with COPD.[6-10] Despite being distinct diseases, overlap exists regarding pathophysiologic features, presentation of acute exacerbations, and management of asthma and COPD among adult patients who are critically ill. This *CHEST Critical Care* Review examines the diagnosis and management of patients who are critically ill with these common conditions.

Evidence Review

Definition and Triggers

Asthma exacerbations are defined as episodes of increased symptoms (eg, shortness of breath, cough, wheezing) and progressive decrease in lung function that require a change in treatment.[11] Similarly, COPD exacerbations are episodes of increased dyspnea, cough, and sputum production, often accompanied by tachypnea, tachycardia, or both, that worsen within 2 weeks from symptom onset.[12] These heterogenous events are caused by complex interactions between a trigger and the patient's immune response.[11-13] Viruses are implicated in 40% to 50% of asthma and COPD exacerbations, and virus-induced COPD exacerbations are associated with increased health care use and a prolonged course.[13-18] Bacterial infections are thought to be a more important trigger for COPD exacerbations; however, uncertainty remains around the role of bacteria in both diseases, particularly severe asthma exacerbations in which bacterial infections have been identified more frequently.[13-16,19-22] In addition, environmental or food allergens can trigger asthma exacerbations, and recognition has been growing around the importance of air pollution and extreme heat in inducing both asthma and COPD exacerbations.[11,23-25]

Initial Evaluation

Asthma and COPD exacerbations are clinical diagnoses without disease-specific confirmatory laboratory or radiographic findings. Thus, it is important to consider other diseases that can mimic or precipitate an exacerbation, including pneumonia, pulmonary embolism, pneumothorax, heart failure, and myocardial infarction, as well as less common conditions such as anaphylaxis, angioedema, or vocal cord dysfunction.[11,12] Table 1[11,12,26-29] outlines the initial evaluation of asthma and COPD exacerbations. Pulse oximetry is the primary method used to assess oxygenation, recognizing it may overestimate blood oxygen content among patients with darker skin tones, but an arterial blood gas assessment should be considered in select patients.[26–28] Sputum bacterial culture and viral pathogen testing are indicated in both asthma and COPD exacerbations, although bacterial culture results should be interpreted with caution because colonization can occur in both severe asthma and COPD.[19,30]

Assessing Severity: After confirming the diagnosis, a clinician should consider the severity of the exacerbation to guide management (Table 1). Severity of an asthma exacerbation is defined by changes in vital signs.[11] Severity of COPD exacerbation was defined historically by the treatments used with severe disease requiring an emergency department (ED) visit or hospitalization; however, the Global Initiative for Chronic Obstructive Lung Disease report now recommends using objective data first outlined in the 2021 Rome Proposal that more closely mirrors severity grading of asthma exacerbations (Table 1).[12,30] Major differences between the definitions of severe disease are the focus on peak expiratory flow and FEV_1 in asthma (severe disease being defined as a peak expiratory flow or FEV_1 of ≤ 40%-50% predicted or best measurement and life-threatening asthma as < 25%) and the incorporation of an elevated C-reactive protein level and acute hypercapnia in severe COPD exacerbations.[11,12,30,31]

TABLE 1] Initial Evaluation and Severity Assessment

Initial evaluation
Pulse oximetry to assess Spo_2 and heart rate
ABG if fatigue or somnolence concerning for hypercapnia, PEF or FEV_1 < 50% predicted, or other clinical concern
Testing for respiratory viral pathogens
Sputum bacterial culture
Initial chest radiograph, ECG, and BNP
Clinical assessment for PE, consider D-dimer or CTA on case-by-case basis
Defining severe exacerbations
Asthma
Respiratory rate > 30 breaths/min
Heart rate > 120 beats/min
Spo_2 < 90% on ambient air
PEF ≤ 50% patient's predicted or best
COPD
Respiratory rate ≥ 24 breaths/min
Heart rate ≥ 95 beats/min
Spo_2 < 92% on ambient air (or home oxygen), change > 3% (when known), or both
Dyspnea VAS ≥ 5
CRP ≥ 10 mg/L

The table outlines similarities and differences in the initial evaluation and definition of severe asthma and COPD exacerbations.[11,12] The definition of a severe asthma exacerbation is based on the Global Initiative for Asthma 2024 report, and the definition of a severe COPD exacerbation was outlined first by the 2021 Rome Proposal and then adopted by the GOLD report.[12,30] Severe disease in asthma requires at least 1 criteria, whereas in COPD, the patient must exhibit at least 3 of 5 criteria plus acute hypercapnia (ABG with $Paco_2$ > 45 mm Hg and pH < 7.35). Dyspnea VAS is a numerical scale from 0 (no shortness of breath) to 10 (maximum shortness of breath ever experienced).[30] ABG = arterial blood gas; BNP = B-type natriuretic peptide; CRP = C-reactive protein; CTA = CT imaging angiography; GOLD = Global Initiative for Chronic Obstructive Lung Disease; $Paco_2$ = arterial carbon dioxide tension; PE = pulmonary embolism; PEF = peak expiratory flow; Spo_2 = oxygen saturation; VAS = visual analog scale.

Pathophysiologic Features of Exacerbations

Asthma often is mediated by activated T-helper 2 cells, mast cells, and eosinophils, whereas COPD exhibits predominantly type 1 cytotoxic cells, macrophages, and neutrophils.[32,33] However, substantial overlap exists between these two inflammatory states: COPD can be eosinophilic predominant, and severe asthma exacerbations commonly demonstrate mixed eosinophilic and neutrophilic inflammation.[12,32-36]

During an exacerbation, the inflammatory response typically progresses over several days, causing microvascular permeability and airway swelling.[37-39] In addition, airway resistance increases because of bronchospasm, a more prominent feature of asthma exacerbations, and mucus plugging within the small airways.[37-40] Increased airway resistance may be compounded by an expiratory flow limitation, whereby airways close prematurely because of reduced elastic recoil (Fig 1A).[12,38,41] The resultant airflow obstruction in asthma and COPD exacerbations causes a ventilation/perfusion ($\dot{V}/\dot{Q}$) mismatch and increases the expiratory time constant, or the time required to exhale 63% of the tidal volume (V_T), calculated as lung resistance × compliance.[42] The longer time constant may prevent return of the alveolar pressure to atmospheric pressure (ie, alveolar pressure remains positive throughout the respiratory cycle) and may cause progressive gas trapping and dynamic hyperinflation in the setting of tachypnea (Fig 1A).[38,41,43] Dynamic hyperinflation reduces the compliance of the lung, which is now operating near the top of the pressure-volume curve, and the mechanical efficiency of the diaphragm, which is now flattened, leading to an unfavorable length-tension relationship and increased respiratory muscle work.[38,41,44,45] Eventually, this mechanical disadvantage can lead to fatigue and respiratory failure. Thus, the primary goals of treatment are to reduce airway inflammation, to reverse bronchospasm, and in severe cases, to offload respiratory muscles with mechanical ventilation (noninvasive or invasive) to support the patient while awaiting improvement in airway inflammation.

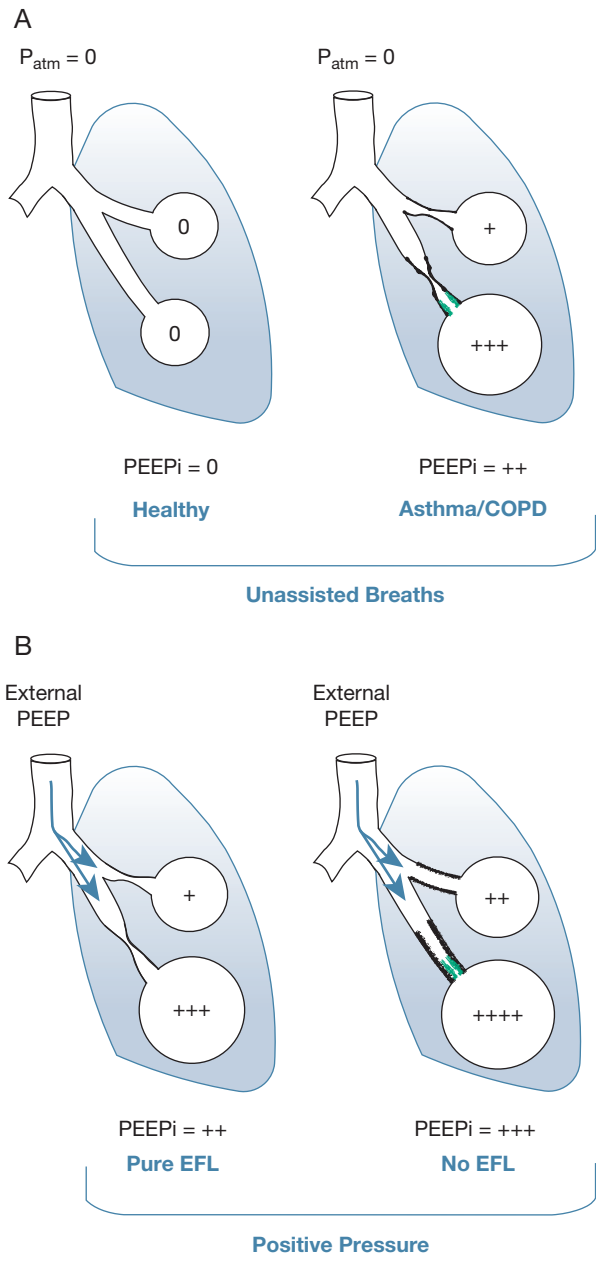

Figure 1 – *Diagram showing physiologic changes that can occur during asthma and COPD exacerbations with unassisted breathing and after the application of external PEEP. A, During unassisted respirations in healthy adults, alveolar pressure equilibrates to P_{atm} at end expiration and flow ceases. During a severe asthma or COPD exacerbation, airway inflammation, bronchospasm, and in some patients an EFL (ie, premature airway closure resulting from reduced elastic recoil) cause a prolonged expiratory time that can prevent alveolar pressure from returning to P_{atm}, resulting in a positive alveolar pressure at end expiration (ie, PEEPi). Lungs often exhibit heterogeneity with units having different PEEPi based on their time constants. B, Response to external PEEP will vary depending on the presence of an EFL. In a pure EFL, the application of external PEEP up to 80% of PEEPi does not change total PEEP or dynamic hyperinflation. This is explained by the waterfall effect, in which the application of pressure downstream from the site of critical closure within the EFL does not impact upstream pressure (ie, PEEPi) or flow until the downstream pressure equals the critical closing pressure, analogous to variations in the level of a river below a waterfall not impacting the flow over a waterfall as long as the river does not exceed the height of the waterfall itself.[189,190] If an EFL is not present, external PEEP will be transmitted to the alveoli, worsening PEEPi and dynamic hyperinflation. A paradoxical decrease in total PEEP in response to external PEEP (not visualized) also has been described, thought to be a result of an EFL and heterogenous lungs. + represents increased pressure above atmospheric pressure with more + signs indicating higher pressure. EFL = expiratory flow limitation; P_{atm} = atmospheric pressure; PEEP = positive end-expiratory pressure; PEEPi = intrinsic positive end-expiratory pressure.*

Inhaled Bronchodilators

The cornerstone in management of asthma and COPD exacerbations is inhaled bronchodilators to treat bronchial hyperreactivity and to reduce airflow obstruction (Table 2). First-line therapy is short-acting β-agonists (SABAs).[11,12] SABAs can be delivered equally effectively using a metered-dose inhaler with a spacer device, with a dry power inhaler, or via a nebulizer; however, nebulized administration may be preferred for patients who are in respiratory distress or who are unable to cooperate with inhalers.[11,12,46-49] Adult patients who are critically ill with severe exacerbations should be treated with short-acting muscarinic antagonists (SAMAs) in addition to SABAs.[11,12] In severe asthma exacerbations managed in the ED, the combination of SABAs and SAMAs resulted in greater improvement in peak expiratory flow to FEV_1 ratio and fewer hospitalizations compared with SABA treatment alone.[50,51] No quality studies have evaluated the role of SAMAs in COPD exacerbations or among patients in the ICU; however, they are recommended for severe exacerbations.[11,12,52]

Corticosteroids

Systemic corticosteroids are an important therapy for severe asthma and COPD exacerbations, and their use is recommended for patients who do not respond to initial bronchodilator therapy (Table 2).[11,12,53] Interestingly, although corticosteroids are recommended for both diseases, their benefit in COPD exacerbations seems to be driven by a subpopulation with high T2 inflammation and elevated eosinophil counts, drawing interest in using eosinophil levels to guide steroid administration among patients who are not critically ill.[12,54-56]

Strong evidence supports corticosteroids for asthma and COPD exacerbations treated in the acute care setting.[57-62] Few studies have evaluated corticosteroids in adult patients who are critically ill with asthma exacerbations, particularly those necessitating mechanical ventilation.[63] For COPD exacerbations requiring mechanical ventilation (either noninvasive ventilation [NIV] or invasive mechanical ventilation

TABLE 2] Pharmacotherapy for Severe Asthma and COPD Exacerbations Managed in the ICU

Pharmacotherapy	Mechanism of Action	Asthma		COPD		Comments
		Indication	Regimen	Indication	Regimen	
Indicated						
SABA	Bronchodilation and smooth muscle relaxation by stimulating airway β_2 receptors	All patients	• MDI/DPI with spacer: albuterol 4-8 inhalations every 20 min for 3 doses, then 2-4 inhalations every 1-4 h • Nebulizer: albuterol 2.5-5 mg every 20 min for 3 doses, then 2.5-5 mg every 1-4 h	All patients	• MDI/DPI with spacer: albuterol 4 inhalations every hour for 3 doses, then 2-4 inhalations every 2-4 h • Nebulizer: albuterol 2.5 mg every hour for 3 doses, then 2.5 mg every 2-4 h	• Albuterol and levalbuterol have similar outcomes and safety profiles; albuterol is recommended as first-line agent • MDI/DPI with spacer and nebulizers provide similar benefit; nebulizer may be preferred in patients who are critically ill or unable to cooperate with inhalers • For COPD, nebulizers should be driven by air, rather than oxygen, to avoid worsening hypercapnia via overoxygenation • Transition nebulizers to inhalers as soon as patient is stabilized to promote teaching and earlier hospital discharge
SAMA	Bronchodilation and smooth muscle relaxation by inhibiting muscarinic acetylcholine receptors	All patients	• MDI with spacer: ipratropium 17 μg/actuation 4-8 inhalations every 20 min for 3 doses, then every 1-4 h • Nebulizer: ipratropium 0.5 mg every 20 min for 3 doses, then every 1-4 h	All patients	• MDI with spacer: ipratropium 17 μg/actuation 2-4 inhalations every hour for up to 3 doses, then every 2-4 h • Nebulizer: ipratropium 0.5 mg every hour for up to 3 doses, then every 2-4 h	• MDI/DPI with spacer and nebulizers provide similar benefit; nebulizer may be preferred in patients who are critically ill or unable to cooperate with inhalers • For COPD, nebulizers should be driven by air, rather than oxygen, to avoid worsening hypercapnia via overoxygenation • Transition nebulizers to inhalers as soon as patient is stabilized to promote teaching and earlier hospital discharge

(Continued)

TABLE 2] *(Continued)*

Pharmacotherapy	Mechanism of Action	Asthma		COPD		Comments
		Indication	Regimen	Indication	Regimen	
Corticosteroids	Inhibit gene transcription of inflammatory mediators, prevent recruitment of eosinophils to the airways, and induce eosinophil apoptosis	All patients	Prednisone 1 mg/kg/d up to 50 mg/d or equivalent for 5-7 d	All patients	Prednisone 40 mg/d or equivalent for 5 d	• Higher doses can be considered on case-by-case basis; very high doses (methylprednisolone $>$ 240 mg/d) should be avoided because of worse outcomes • Corticosteroids with primarily glucocorticoid effects (eg, prednisone or methylprednisolone) generally preferred over those with mineralocorticoid effects (eg, hydrocortisone, dexamethasone) as more extensively studied, although any formulation can be used • PO and IV formulations have similar bioavailability • PO recommended for most patients because of quicker onset and lower cost
Adjunct therapies						
Antibiotics	Bacteria eradication by inhibiting synthesis of nucleic acids, proteins, or cell wall	Concern for concurrent lung infection	Aminopenicillin with clavulanic acid, macrolide, tetracycline, or equivalent coverage for community acquired pneumonia for 5-7 d	• Increased dyspnea, sputum volume, and sputum purulence (need all 3 or 2 if sputum purulence is present) or • Patients requiring NIV or IMV	Aminopenicillin with clavulanic acid, macrolide, or tetracycline for 5-7 d	• Consider antipseudomonal agent (eg, quinolone) if risk factors for *Pseudomonas*: chronic colonization, FEV_1 $<$ 50%, bronchiectasis, chronic steroid use

(Continued)

TABLE 2] *(Continued)*

Pharmacotherapy	Mechanism of Action	Asthma		COPD		Comments
		Indication	Regimen	Indication	Regimen	
IV magnesium	Bronchodilation by inhibiting calcium channels within bronchial smooth muscle and blocking parasympathetic tone in the tracheobronchial tree	Consider for exacerbations nonresponsive to initial therapies	Single dose of 2 g administered over 20 min	Consider for exacerbations nonresponsive to initial therapies	Single dose of 2 g administered over 20 min	• IV magnesium associated with reduced hospital admissions in adults with asthma or COPD • May enhance the bronchodilator effects of SABAs • Very limited data for use among who are critically ill and hospitalized
IV ketamine	Bronchodilation, thought to be independent from NMDA receptors, although exact mechanism debated	Limited data to support use, consider on case-by-case basis	0.2-0.5 mg/kg IV bolus administered over 5 minutes followed by 0.05-0.25 mg/kg/h infusion	Not indicated because of paucity of data	N/A	• Small RCTs demonstrated mixed results compared with placebo for asthma exacerbations • Nonintubated patients need to be monitored closely because of the risk of respiratory depression • Can consider higher doses (0.5-2 mg/kg/h) among patients receiving IMV
Helium-oxygen	Lower density of helium decreases airway resistance, promotes laminar flow, and decreases work of breathing	Limited data to support use, consider on case-by-case basis	Mixture of 70%-80% helium and 20%-30% oxygen	Limited data to support use, consider on case-by-case basis	Mixture of 70%-80% helium and 20%-30% oxygen	• Among asthma exacerbations, greatest improvement in pulmonary function occurred in patients with the most severe pulmonary function impairment • Minimal data on clinical outcomes in asthma exacerbations • Improved respiratory mechanics and statistically insignificant trend toward lower NIV failure in COPD exacerbations

(Continued)

TABLE 2] *(Continued)*

Pharmacotherapy	Mechanism of Action	Asthma		COPD		Comments
		Indication	Regimen	Indication	Regimen	
Volatile anesthetic	Bronchodilation via smooth muscle relaxation, thought to be from several different mechanisms	Limited data to support use, consider on case-by-case basis	• Sevoflurane: 1.4%-2.6% • Desflurane: 2.5%-8.5% • Isoflurane: 1.0%-3.0%	Not indicated because of paucity of data and lack of efficacy	N/A	• Very limited prospective data in asthma exacerbations; may improve respiratory mechanics • Studies in COPD exacerbations showed mixed effects on respiratory mechanics compared with IV sedation
Biologics	Reduction in airway inflammation by inhibiting IgE or IL-5	Limited data to support use, consider on case-by-case basis	• Omalizumab 150-375 mg SQ • Mepolizumab 100 mg SQ • Benralizumab 30 mg SQ	Not indicated because of paucity of data	N/A	• Use in severe asthma exacerbations primarily limited to case reports • Omalizumab dose varies based on actual body weight • Unclear if newer biologics (eg, dupilumab, tezepelumab) can be used in a similar manner
Not indicated						
Methylxanthines	Bronchodilation by inhibiting phosphodiesterase 3 and antiinflammatory properties	Not indicated because of lack of efficacy and increased adverse events	N/A	Not indicated because of paucity of data and increased adverse events	N/A	• Does not improve outcomes compared with SABAs alone in asthma or COPD exacerbations • Narrow therapeutic window • Associated with increased adverse events, including nausea, emesis, palpitations, and tachyarrhythmias
Terbutaline	Bronchodilation and smooth muscle relaxation by stimulating β_2 receptors	Not indicated because of paucity of data and lack of efficacy	N/A	Not indicated	N/A	• Low-quality evidence; does not improve outcomes compared with SABAs alone in asthma exacerbations

The table provides information and recommendations on pharmacotherapies for severe asthma and COPD exacerbations among patients who are critically ill adult.[11,12,31,46-53,57-84,89-110,134,191-197] DPI = dry powdered inhaler; IMV = invasive mechanical ventilation; MDI = metered-dose inhaler; NA = not applicable; NIV = noninvasive ventilation; NMDA = N-methyl-D-aspartate; RCT = randomized controlled trial; SABA = short-acting β-agonist; SAMA = short-acting muscarinic antagonist; SQ = subcutaneous.

[IMV]), one study found that corticosteroids were associated with a reduction in duration of IMV and rate of NIV failure, whereas another study found no difference in outcomes.[64,65]

Among patients managed in acute care settings, the recommended regimen is prednisone 1 mg/kg/d up to 50 mg/d or equivalent for 5 to 7 days for asthma and prednisone 40 mg/d for 5 days for COPD based on studies showing shorter courses (5-7 days vs 10-14 days) resulted in similar rates of treatment failure and relapse with reduced risk of pneumonia and death.[11,12,66-70] Of the few studies conducted in patients who are critically ill, most used higher doses.[63,64] However, very high doses (ie, methylprednisolone > 240 mg/d) have been associated with increased treatment failure, duration of IMV, ICU and hospital length of stay (LOS), and adverse events, including hyperglycemia requiring insulin therapy and fungal infections.[71] Currently evidence to suggest routine use of higher corticosteroid doses is limited, and we recommend prednisone 40 to 50 mg/d for at least 5 days with consideration of higher doses in patients with life-threatening disease or those not responding to initial therapy.

Antibiotics

Studies investigating the role of antibiotic therapy in asthma exacerbations, none of which included patients in the ICU, found no difference in symptoms or lung function with the addition of antimicrobials.[72] A more recent large retrospective study of early antibiotic treatment among patients hospitalized for asthma exacerbations showed a reduction in a composite measure of treatment failure, defined as initiation of IMV, transfer to the ICU, hospital mortality, and readmissions.[73,74] Treating clinicians should administer antibiotics to patients with asthma exacerbations who are critically ill if concerned about a concurrent lung infection; however, data to support a standard regimen of antibiotics in this population are limited, consistent with the Global Initiative for Asthma recommendations for hospitalized patients.[11]

Antimicrobial therapy should be given to patients with COPD exacerbations who are critically ill who exhibit increased dyspnea, sputum volume, or purulence (either all 3 symptoms required or 2 symptoms if sputum purulence is present) or those requiring mechanical ventilation (NIV or IMV).[12,75] Antibiotics decrease the risk of treatment failure and mortality in patients hospitalized with COPD exacerbations, driven by a subset of patients who exhibit increased sputum purulence, which may be a surrogate for bacterial load.[12,76-81] Macrolides or tetracyclines are mainstay options, although an antipseudomonal agent should be considered for patients with risk factors for *Pseudomonas* (Table 2).[12,82-84] Antibiotics should be continued for 5 to 7 days as longer courses have not been shown to change clinical outcomes.[12,75] Currently, evidence is insufficient to implement routine use of biomarkers (ie, C-reactive protein or procalcitonin) to determine antibiotic administration.[11,12,85-88]

Other Medications

IV magnesium sulfate has been shown to reduce hospitalizations among patients with life-threatening asthma exacerbations and COPD exacerbations in the ED, and it should be considered in patients not responding to initial therapies (Table 2).[11,89-91] The use of ketamine, a dissociative analgesic with bronchodilator effects, has been suggested in patients who are not intubated at low, subdissociative doses; however, quality data showing a clinical benefit are lacking.[92,93] Some interest exists in using biologic agents in asthma exacerbations, given their relatively quick onset over days, although data have been limited to case reports and 1 randomized controlled trial (RCT) demonstrating that benralizumab administered in the ED reduced the rate of recurrent exacerbations in the subsequent 12 weeks.[94,95] Methylxanthines (eg, theophylline and aminophylline) and terbutaline, an IV β_2-agonist, are not recommended for asthma or COPD exacerbations among adults because of their lack of efficacy compared with inhaled β_2-agonists, and methylxanthines are associated with increased side effects and adverse events such as tachyarrhythmias.[11,12,31,96-98]

Inhaled Gases

The use of volatile anesthetics for life-threatening asthma exacerbations has been described in case reports, although prospective data are insufficient to support their use outside of refractory cases of bronchospasm until further research is carried out.[99-101] No role currently exists for volatile anesthetics in severe COPD exacerbations because studies show mixed effects on respiratory mechanics compared with IV sedation.[102,103] Helium-oxygen (heliox) mixtures, used to promote laminar flow and to reduce airway resistance, may improve respiratory mechanics during severe asthma exacerbations, although data are limited on meaningful clinical outcomes in this population.[104-106] Among COPD exacerbations requiring NIV or IMV, heliox improves the work of breathing and intrinsic positive

end-expiratory pressure (PEEPi). Two RCTs of COPD exacerbations requiring NIV found that heliox did not prevent NIV failure; however, trends toward lower intubation rates and greater time to NIV failure were noted in the heliox group.[107-110] Heliox could be considered on a case-by-case basis as an adjunct therapy for patients with severe asthma and COPD exacerbations refractory to other treatments.

Supplemental Oxygen

Many patients managed in the ICU with life-threatening exacerbations will demonstrate hypoxemia resulting from $\dot{V}/\dot{Q}$ mismatch. Hypoxemia typically is mild in asthma, even during life-threatening exacerbations, and a Pa_{O_2} of $<$ 55 mm Hg or a required F_{IO_2} of $>$ 30% to 50% should prompt evaluation for additional causes.[111] Supplemental oxygen should be initiated and titrated to a target oxygen saturation of 93% to 95% in asthma and 88% to 92% in COPD.[11,12,112-114] Administration of excess oxygen can promote hypercapnia because of worsening $\dot{V}/\dot{Q}$ mismatch and the offloading of CO_2 from hemoglobin as a result of the Haldane effect, in which CO_2 bound to hemoglobin is removed when hemoglobin becomes oxygenated.[115] More importantly, hyperoxia is associated with increased mortality in COPD exacerbations.[113,114]

High-Flow Nasal Therapy

High-flow nasal therapy (HFNT) delivers heated and humidified oxygen through a nasal cannula at flow rates up to 60 L/min (Fig 2).[116] HFNT more accurately delivers high F_{IO_2} compared with conventional oxygen therapy, improves CO_2 elimination by washing out CO_2 from the upper airways, where gas exchange does not occur (ie, anatomic dead space), and generates a low level of positive pressure that may recruit atelectatic lung and improve both $\dot{V}/\dot{Q}$ mismatch and lung compliance.[116-118] One small RCT comparing HFNT with conventional oxygen therapy in severe asthma exacerbations complicated by respiratory failure showed that HFNT improved oxygenation, heart rate, and respiratory rate without a differential change in Pa_{CO_2}.[119] Otherwise, data on HFNT for severe asthma exacerbations are very limited, particularly studies evaluating clinical outcomes such as the need for mechanical ventilation and mortality, and its use should be considered experimental at this time.[119,120]

Among patients with COPD exacerbations or stable COPD, HFNT improves patient comfort, work of breathing, and alveolar ventilation.[121] The few studies evaluating HFNT vs conventional oxygen therapy for COPD exacerbations found that HFNT did not reduce the need for NIV or IMV or mortality.[122,123] Several small studies comparing HFNT with NIV in the treatment of COPD exacerbation with moderate hypercapnia (pH, 7.25-7.35; $Pa_{CO_2} \geq$ 50-55 mm Hg) found a similar reduction in Pa_{CO_2}, treatment failure rates, and mortality; however, almost one-third of patients receiving HFNT required NIV within 6 hours in one study.[124-126] More recently, a larger noninferiority RCT in the same population showed that HFNT was associated with a higher rate of treatment failure and intubation, but no difference in ICU or hospital LOS or mortality compared with NIV.[127] Additional large RCTs are needed to understand better the role of HFNT in both asthma and COPD exacerbations. Currently, NIV should be considered before HFNT for severe COPD exacerbations with respiratory acidosis; however, HFNT may be an alternative in patients who do not tolerate NIV, would benefit from alternating between these methods, or both.[128]

Noninvasive Mechanical Ventilation

NIV counteracts several aspects of the dysfunctional pathophysiologic characteristics exhibited during exacerbations. NIV recruits alveoli through the application of external positive end-expiratory pressure (PEEP).[129] In addition, external PEEP offloads the inspiratory muscles by reducing the negative inspiratory force needed to overcome PEEPi, or the positive alveolar pressure at end-expiration resulting from dynamic hyperinflation, and triggers an assisted breath.[38,129] The pressure support delivered in addition to PEEP also promotes greater V_T, which ultimately increases alveolar ventilation.[38,129] The result is an improvement in hypercapnia, hypoxemia, and work of breathing.

The role of NIV in severe asthma exacerbations remains poorly defined, and Global Initiative for Asthma guidelines do not provide a recommendation on its use.[11] A limited number of small RCTs showed that NIV improves lung function parameters and ICU and hospital LOS.[130] Retrospective studies, one of which included $>$ 53,000 participants, found that NIV was associated with reduced mortality and need for IMV.[131,132] Despite the paucity of RCTs, use of NIV for asthma has increased over the last few decades,

	Supplemental O_2	HFNT	NIV	IMV	VV ECMO
Indications	Spo_2 < 92% in asthma Spo_2 < 88% in COPD	Severe dyspnea with respiratory distress (eg, accessory muscle use) Persistent hypoxemia despite O_2	Severe dyspnea with respiratory distress Persistent hypoxemia despite O_2 $PaCO_2$ ≥ 45 mmHg and pH ≤ 7.35	Cardiac arrest/HD instability Inability to tolerate NIV or worsening respiratory failure despite NIV Altered consciousness Massive aspiration or persistent vomiting	Hypercapnic respiratory failure (pH < 7.25) despite optimal IMV Hypoxemic respiratory failure despite optimal IMV Hemodynamic compromise from hyperinflation
Initial Settings	Titrate 1-15 L/min flow to target Spo_2 93%-95% in asthma and Spo_2 88%-92% in COPD	Flow 15-60 L/min; use higher flow to obtain a PEEP of 3-5 cm H_2O Titrate Fio_2 to target Spo_2 93%-95% in asthma and Spo_2 88%-92% in COPD	Titrate PS to target V_T of 6-8 mL/kg IBW Initial PEEP approximately 5 cm H_2O Titrate Fio_2 to target Spo_2 93%-95% in asthma and Spo_2 88%-92% in COPD	V_T 6-8 mL/kg RR, 10-12 breaths/min PEEP, 0-10 cm H_2O Titrate Fio_2 to Spo_2 goal I:E ratio between 1:2 and 1:4 Flow rate, 60-100 L/min Trigger sensitivity, −1 to −2 cm H_2O or 2 L/min[a]	Titrate 2-6 L/min flow to Spo_2 goal Titrate FDO_2 to Spo_2 goal Sweep 1-9 L/min, titrate to reduce $PaCO_2$ by < 20 mmHg in first 24 h
Complications	Hyperoxia associated with increased mortality in COPD Epistaxis	Claustrophobia/discomfort Impaired swallow function and risk of aspiration	Claustrophobia/discomfort Skin breakdown at mask interface Gastric distention/risk of aspiration	Barotrauma (eg, pneumothorax) Ventilator-associated pneumonia ETT complications (eg, tracheal stenosis) Muscle weakness	Hemorrhage Thrombosis Infection Cannulation complications (eg, vascular perforation)

Figure 2 – *Diagram outlining the indications, initial settings, and complications of the various respiratory support methods that can be used during a severe asthma or COPD exacerbation.*[11,12,43,112-115,128,143,150,159,172-175] [a]*Trigger sensitivity should be set to −1 to −2 cm H_2O with pressure triggering or 2 L/min with flow triggering. ABG = arterial blood gas; ETT = endotracheal tube; FDO_2 = fractional delivered oxygen; HD = hemodynamic; I:E = inspiratory to expiratory; IBW = ideal body weight; IMV = invasive mechanical ventilation; NIV = noninvasive ventilation; $Paco_2$ = arterial carbon dioxide tension; PEEP = positive end-expiratory pressure; PS = pressure support; RR = respiratory rate; Spo_2 = oxygen saturation; V_T = tidal volume; VV ECMO = venovenous extracorporeal membrane oxygenation.*

accompanied by a shift away from IMV, without a resultant change in mortality or hospital LOS.[133] We believe a trial of NIV can be attempted for most severe asthma exacerbations managed in the ICU, with caution in those patients with life-threatening exacerbations.

NIV is the preferred initial method of mechanical ventilation for acute respiratory failure during COPD exacerbations.[12,52,134] NIV improves hypoxemia, hypercapnia, and work of breathing via the mechanisms discussed above, and it reduces the need for intubation, mortality, and ICU and hospital LOS, while also being associated with lower rates of nosocomial pneumonia.[12,134,135] Indications, contraindications, and potential complications of NIV are outlined in Figure 2.[12,136] Initial settings depend on patient characteristics; however, basic principles include titrating PEEP to improve work of breathing while not worsening hyperinflation (see Invasive Mechanical Ventilation section) and setting pressure support to target a V_T of approximately 6 to 8 mL/kg ideal body weight. Patients should be monitored regularly, particularly early in the course, using physical examinations and blood gas assessments to guide settings. For patients with persistent hypercapnia despite initial application of NIV, the pressure support can be uptitrated to increase V_T and minute ventilation. Sedative or analgesic medications (eg, opioids or benzodiazepines) are used commonly to manage discomfort or anxiety associated with NIV, and dexmedetomidine, an α_2-adrenergic agonist, is an attractive sedative agent in this setting given its lack of respiratory depression and potential to reduce the risk of intubation and ICU LOS.[137,138] However, data on the safety of sedative and analgesic medications during NIV are mixed, with a particular risk of harm when combining agents from different medication classes, and these drugs should be used sparingly until additional RCTs clarify their role.[137-140]

Although the benefits of NIV in COPD exacerbations are evident, it is important to note that in 20% to 30% of patients, NIV will fail and they will require IMV.[12,141,142] Risk factors for NIV failure include older age, higher

BMI, higher Acute Physiology and Chronic Health Evaluation II score, and persistent hypoxemia and hypercapnia despite 1 hour of NIV.[143-145] Particular attention should be paid to these high-risk patients to identify signs of early treatment failure. In addition a risk score that incorporates heart rate, acidosis, consciousness, oxygenation, and respiratory rate, abbreviated as the HACOR score based on its components, can be used to help predict NIV failure among patients experiencing a COPD exacerbation.[146] Diaphragmatic dysfunction, defined as a change in diaphragm thickness of < 20% on ultrasound during VT, may predict NIV failure, but its usefulness in this setting remains an area of ongoing research.[147,148]

Invasive Mechanical Ventilation

Despite maximum noninvasive therapies, 1% to 2% of patients hospitalized with asthma and COPD exacerbations will require IMV.[4,133,149] Indications and complications for IMV are outlined in Figure 2.[12,150] The decision to pursue IMV should be discussed with the patient or a health care proxy if the patient lacks decision-making capacity. Importantly, health care providers often underestimate the chance of survival for patients with COPD exacerbation requiring IMV, despite these patients having favorable outcomes compared with other causes of respiratory failure.[6,151]

Preoxygenation should be undertaken before intubation if time allows. The positive pressure delivered during IMV may worsen existing high intrathoracic pressure because of dynamic hyperinflation, which can result in decreased venous return and periprocedural hypotension. Therefore, hemodynamics should be optimized before intubation with fluid resuscitation and vasopressors such as norepinephrine.[152] Patients with severe obstructive lung disease, particularly those with preprocedure hypoxemia, should be considered as having physiologically difficult airways due to the risks of periprocedural hypoxemia and cardiovascular collapse from high intrathoracic pressure impairing venous return to the right side of the heart.[152-155] Commonly, rapid sequence intubation is used, with a sedative and paralytic agent given simultaneously. Another alternative is delayed sequence intubation, in which the induction agent is separated from the paralytic to allow additional time for preoxygenation.[152] Ketamine and propofol are the preferred agents for induction and continuous sedation during mechanical ventilation because of their bronchodilator effects, the former causing less hypotension.[156,157] Intubation should be completed with the largest diameter endotracheal tube appropriate for the size of the patient (eg, 7.5-8 mm) to reduce airway resistance and peak pressures, to facilitate suctioning and bronchoscopy if needed, and possibly to improve mortality.[152,158]

The initial phase of IMV should focus on limiting hyperinflation, rather than attempting to normalize blood gases, and permissive hypercapnia (pH, 7.25-7.30) is encouraged.[43,150,159] A control method should be used, with no clear superiority of volume vs pressure methods.[160] Ventilatory settings aimed at minimizing hyperinflation will use a lower minute ventilation and an extended expiratory time with low inspiratory to expiratory ratio to allow time for expiration. Initial settings will approximate the following: VT, 6 to 8 mL/kg ideal body weight; respiratory rate (RR), 10 to 12 breaths/min; PEEP, 0 to 10 cm H_2O; inspiratory to expiratory ratio between 1:2 and 1:4; inspiratory flow rate, 60 to 100 L/min; and trigger sensitivity, –1 to –2 cm H_2O with pressure triggering and 2 L/min with flow triggering.[43,143,150,159] Optimal initial PEEP will vary based on patient characteristics; however, we suggest starting at 5 cm H_2O (or 50%-80% of PEEPi if it is known) and titrating based on patient response as discussed herein.

Patients with severe airflow obstruction are at high risk of ventilator-associated complications resulting from barotrauma and dynamic hyperinflation. Assessment for hyperinflation should be completed regularly by measuring the plateau airway pressure (P_{plat}) and PEEPi (Fig 3).[43,143,159] P_{plat} is measured in a volume control mode via an inspiratory hold maneuver in which a set VT is delivered and then airflow is stopped, allowing the measured pressure in the ventilator circuit to equilibrate to alveolar pressure. Peak inspiratory pressure is the highest pressure measured during the inspiratory cycle and is a function of resistance and compliance. P_{plat} is the pressure when flow has stopped and thus measures static compliance, which is a surrogate for the degree of hyperinflation.[160] P_{plat} should remain < 30 cm H_2O to avoid barotrauma.[43] In addition, elevated P_{plat} should prompt an evaluation for other pathologic features within the lung parenchyma and pleural space, such as pulmonary edema, pneumonia, pneumothorax, or pleural effusion. It is important to note that an inspiratory hold measures static compliance and not dynamic compliance, or the lung compliance during normal respirations that is a function of both the lung and chest wall compliance and airflow resistance. Dynamic compliance typically will be lower than the

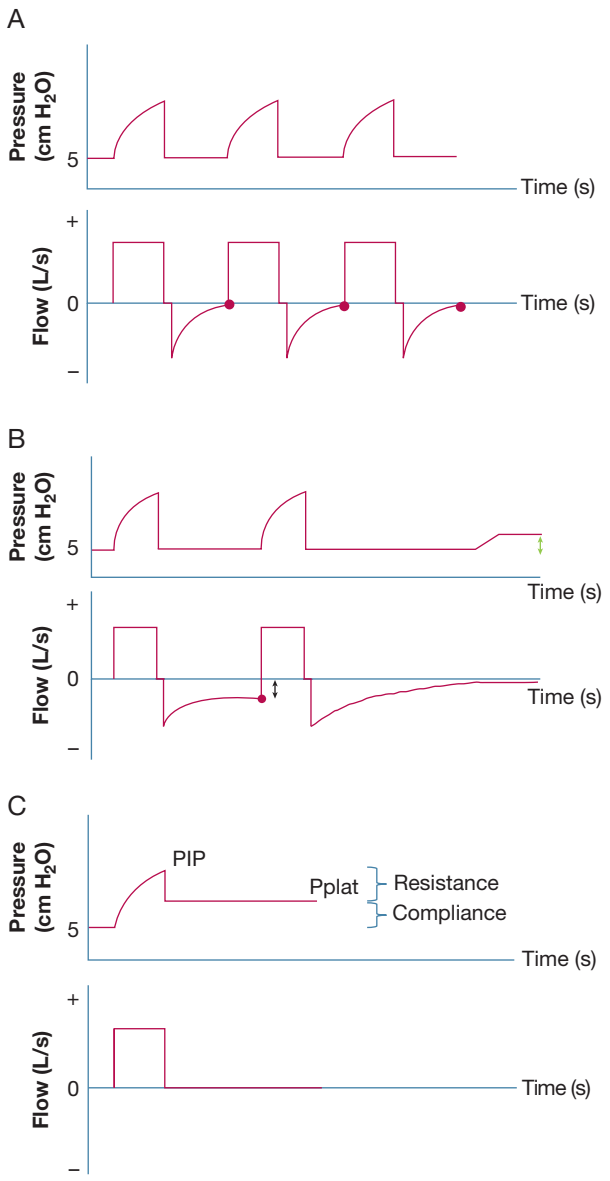

Figure 3 – *A-C, Graphs assessing lung mechanics while receiving ventilation: normal ventilator pressure and flow tracings (A), signs of intrinsic positive end-expiratory pressure (PEEP) and an expiratory hold maneuver (B), and an inspiratory hold maneuver (C). A, Normal flow and pressure tracings in a patient receiving mechanical ventilation in a volume control mode with PEEP set at 5 cm H_2O. Flow reaches 0 L/s before initiation of the next breath (red dot). B, During an exacerbation, prolonged lung emptying may occur as a result of increased resistance and flow limitation (first breath). The flow does not reach 0 L/s before initiation of the second breath (red dot). Therefore, some degree of gas trapping occurs (black arrow), which can be measured by an expiratory hold maneuver (second breath). In this maneuver, the provider toggles a setting that briefly prevents the ventilator from delivering additional breaths. As soon as flow stops (reaches 0 L/s), the pressure in the ventilator circuit equilibrates to alveolar pressure and the total PEEP can be measured. A patient's intrinsic PEEP is the difference between the total PEEP and set PEEP (green arrow). C, In an inspiratory hold maneuver, a set tidal volume is delivered and then flow stops. This allows measurement of the PIP and the Pplat. PIP is the highest pressure experienced during delivery of the breath; it is a function of resistance and compliance. P_{plat} is obtained when flow has stopped (reached 0 L/s), and thus is a measurement only of compliance. Resistance should be elevated in obstructive lung disease, and compliance can be low, normal, or high, depending on the severity of the exacerbation and the patient's underlying physiologic characteristics. Normal resistance and compliance suggest an alternative cause for the respiratory failure. PIP = peak inspiratory pressure; Pplat = plateau pressure.*

measured static compliance in these patients, and it can be increasingly lower in the setting of worsening tachypnea, because airflow obstruction prevents emptying of air from units with longer time constants within the heterogenous lungs.[161]

Another measure of hyperinflation is PEEPi. A flow-time waveform expiratory limb that does not return to baseline between breaths is indicative of PEEPi and should prompt an end-expiratory occlusion maneuver to measure the total PEEP (Fig 3). During this maneuver, the ventilator allows exhalation and then temporarily prevents additional breaths from being delivered, causing the pressure in the ventilator circuit to equilibrate to alveolar pressure. The equilibrated pressure is the total PEEP within the lungs. PEEPi can be calculated by taking the difference between the total PEEP and the set PEEP.

Elevated PEEPi, if present, should be minimized by decreasing the RR, V_T, or inspiratory to expiratory ratio.[43,159] Among these, decreasing the RR has the greatest impact, although its effects are diminished at low respiratory rates (< 8-12 breaths/min) because expiratory flow rapidly decreases after the first few seconds.[43,143] The inspiratory time also can be shortened by increasing the inspiratory flow rate, changing from a decelerating inspiratory flow pattern to a square waveform within a flow-volume targeted ventilator mode, or both.[43,159,160,162] In addition, external PEEP should be titrated to minimize PEEPi while monitoring for changes in total PEEP and P_{plat} as measurements of hyperinflation. Three different responses to increasing external PEEP have been described: (1) no change in total PEEP or P_{plat} with PEEP up to 80% of the PEEPi in patients with an expiratory flow limitation, (2) increased total PEEP and P_{plat} in those without an expiratory flow limitation, and (3) a paradoxical decrease in total PEEP and P_{plat}, possibly resulting from a combination of expiratory flow limitation and heterogenous lungs (Fig 1B).[43,143,159,163] PEEP titration should be stopped if P_{plat} increases.[159] Measurements of P_{plat} and PEEPi can be elevated artificially in patients with spontaneous respiratory effort. In this setting, deep sedation with or without a bolus dose of a neuromuscular blocking agent can be considered if accurate measurements are needed to guide management.[43]

Patients with severe asthma and COPD exacerbations frequently exhibit patient-ventilator dyssynchrony resulting from dynamic hyperinflation and high inspiratory flow demands, and dyssynchrony has been associated with increased work of breathing, worse hyperinflation, and poor clinical outcomes.[164] One of the most common forms is trigger dyssynchrony, in which the patient's inspiratory effort is unable to overcome both the ventilator trigger threshold and PEEPi to trigger a ventilator-assisted breath.[159,160,164] Trigger dyssynchrony can be managed by increasing PEEP to match PEEPi better (among patients who are PEEP responders) or decreasing the trigger threshold.[159,160] Routine administration of neuromuscular blocking agents is not recommended because of the risk of myopathy, particularly with concurrent corticosteroid use; however, these agents can be considered on a case-by-case basis to reduce patient-ventilator dyssynchrony, risk of barotrauma, and oxygen consumption among patients who exhibit persistent dyssynchrony despite ventilator optimization and adequate sedation.[165-168]

Advanced Therapies

Patients with life-threatening exacerbations exhibiting persistent severe hypoxemia, hypercapnia, or hemodynamic compromise resulting from hyperinflation despite IMV optimization should be considered for venovenous ECMO, especially life-threatening asthma exacerbations because of the reversible nature of the disease and high survival rate among those who receive venovenous ECMO (Fig 2).[169-172] Importantly, our understanding of venovenous ECMO in severe obstructive lung disease comes from registry data and case series, rather than RCTs. Guideline-directed criteria for venovenous ECMO initiation in severe obstructive lung disease do not exist, and the decision should be made in consultation with an ECMO specialist. Relative contraindications include increasing age (no specific limit), multiorgan failure, IMV with high settings ($F_{IO_2} > 90\%$ or $P_{plat} \geq 30$ cm H_2O) for ≥ 7 days, bleeding diathesis or contraindication to anticoagulation, or comorbidities such as terminal malignancy.[173]

After cannulation, venovenous ECMO flow rates and the fraction of delivered oxygen should be titrated to obtain goal oxygen saturation. The sweep gas flow should be adjusted to normalize P_{aCO_2} slowly, because a rapid reduction in P_{aCO_2} (> 20 mm Hg or 50% of the pretreatment P_{aCO_2} over 24 hours) has been associated with neurologic complications such as intracranial hemorrhage, ischemic stroke, and brain death.[174,175] In addition, ventilator settings should be reduced to ultra-lung protective settings to allow lung rest. Often, pressure control ventilation is used, targeting P_{plat} of $\leq$ 25 cm H_2O, PEEP of 5 to 10 cm H_2O, and RR of 4 to 15 breaths/min, although these settings are based on studies of acute respiratory distress syndrome and settings may be different in patients with severe obstructive lung disease.[172,173] Additional disease-specific therapies such as bronchodilators and corticosteroids should be continued while a patient is receiving venovenous ECMO.[172]

Extracorporeal CO_2 removal is a novel strategy that provides CO_2 removal without significant oxygenation using smaller cannulas and lower flow rates.[172,176] Among patients with COPD and hypercapnia, extracorporeal CO_2 removal has been studied as a salvage therapy like ECMO or as a method either to prevent intubation or to promote earlier extubation; however, its role remains limited because of insufficient prospective data, a high risk of bleeding, and a lack of impact on mortality.[176-179]

Extubation

Readiness for extubation should be assessed in a similar manner to other respiratory diseases, requiring improvement in the underlying obstructive process necessitating intubation, ability to follow commands during a spontaneous awakening trial, and respiratory stability during a spontaneous breathing trial with minimal pressure support settings.

It remains unknown if patients with severe asthma exacerbations should be extubated to NIV or HFNT. Conversely, patients with COPD exacerbation should be extubated to either NIV with the same settings used during IMV or to HFNT because both methods have been shown to decrease mortality, reintubation rates, and duration of IMV.[180-183] Comparison of NIV and HFNT in COPD exacerbations has shown similar effectiveness, although NIV may be more beneficial in patients who are high-risk.[184-186] Alternating between NIV and HFNT also was more effective than HFNT alone, a method that may be useful in patients who have difficulty tolerating NIV.[187] Importantly, NIV or HFNT should be used immediately after extubation, rather than waiting for recurrent respiratory failure to develop, as

the latter has been associated with increased mortality, possibly because of delayed reintubation.[188]

Future Directions

Life-threatening asthma and COPD exacerbations are encountered commonly in the ICU and are associated with significant morbidity and mortality. It is important to understand both the commonalities and differences in the pathophysiologic features and management of these diseases to provide evidence-based care and improve outcomes. A stepwise treatment approach will aim to reduce airway inflammation, to reverse bronchospasm, and if needed, to support patients with mechanical ventilation or advanced therapies until clinical improvement is achieved.

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CLINICAL QUESTION

A 35-year-old man with a history of poorly controlled asthma seeks treatment at the emergency department because of shortness of breath and chest tightness, diagnosed as an asthma exacerbation. Despite treatment with nebulized bronchodilators and IV corticosteroids, he remains in severe respiratory distress with acute hypercapnia, prompting urgent intubation. His initial ventilator settings in a volume control mode are: tidal volume, 400 mL; respiratory rate, 30 breaths/min; F_{IO_2}, 40%; and positive end expiratory pressure (PEEP), 5 cm H_2O. Shortly after arrival to the ICU, he becomes acutely hypoxemic, hypotensive, and tachycardic. Bedside ultrasound reveals lung sliding bilaterally and normal cardiac function without evidence of tamponade. The endotracheal tube is disconnected from the ventilator, and the patient is allowed to exhale fully. The hemodynamic features improve and the endotracheal tube is reconnected to the ventilator.

Which of the following should be adjusted to prevent this from occurring again?

A. Increase the inspiratory to expiratory ratio B. Decrease the respiratory rate C. Increase the F_{IO_2}

D. Prone positioning

Correct answer: B, Decrease the respiratory rate

The patient seeks treatment with a severe asthma exacerbation and acute hypercapnia requiring intubation. Although it would be preferable to correct the acute respiratory acidosis fully with mechanical ventilation, this can prove challenging because of the airways obstruction and flow limitation caused by the asthma exacerbation. As a result, exhalation time will be prolonged. If another breath is initiated by the ventilator before the end of exhalation, inadequate time for lung emptying can lead to progressive hyperinflation and increased positive pressure within the alveoli throughout the respiratory cycle (ie, intrinsic PEEP). If this continues unchecked, it will cause increased intrathoracic pressure and decreased venous return, which will result in decreased cardiac output and ultimately hypotension and compensatory tachycardia. The most effective way to prevent hyperinflation and intrinsic PEEP in this patient is to lower the respiratory rate. Decreasing the tidal volume or the inspiratory to expiratory ratio (rather than increasing the inspiratory to expiratory ratio; answer choice A) also may be beneficial. Importantly, lowering the respiratory rate or tidal volume reduces the minute ventilation, and as a result, providers likely will need to allow some degree of permissive hypercapnia (pH, 7.25-7.30) while treating the underlying asthma exacerbation.[1]

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